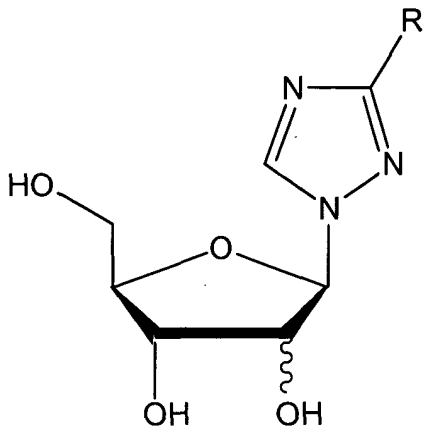
Claims

1. A method of treatment or prophylaxis of an inflammatory bowel disease in a subject in need of said treatment or prophylaxis, said method comprising:

providing one or more ribofuranose derivatives having the Formula (I):



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wherein R is a group selected from the group consisting of a carboxamide, an amidine and pharmaceutically acceptable acid addition salts thereof and the configuration at the C_2 carbon of the ribofuranose moiety is D or L; and

administering said one or more ribofuranose derivatives to said subject in an amount effective to treat or prevent said inflammatory bowel disease.

2. The method of claim 1, wherein the ribofuranose derivative having the Formula (I) comprises at least one derivative selected from the group consisting of 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide, l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide, l-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine, l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine, pharmaceutically acceptable acid addition salts thereof.

3. The method of claim 2, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide.

4. The method of claim 2, wherein the ribofuranose derivative having Formula (I) is l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide.

5. The method of claim 2, wherein the ribofuranose derivative having Formula (I) is l-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

6. The method of claim 2, wherein the ribofuranose derivative having Formula (I) is l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

7. The method of claim 2, wherein the ribofuranose derivative is the hydrochloric acid addition salt of 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

8. The method of claim 2, wherein the ribofuranose derivative is the hydrochloric acid addition salt of l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

9. The method of claim 1, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the inflammatory bowel disease is Crohn's disease.

10. The method of claim 9, wherein said Crohn's disease is selected from the group consisting of active Crohn's disease, refractory Crohn's disease, and fistulizing Crohn's disease.

11. The method of claim 1, wherein the ribofuranose derivative having Formula (I) is provided in combination with an antiviral, wherein the ribofuranose derivative having Formula (I) and the antiviral are administered to said subject simultaneously as an admixture, separately and simultaneously, or separately in any order.

12. The method of claim 11, wherein said antiviral agent is selected from the group consisting of abacavir, acyclovir, acyclovir sodium, acyclovir potassium, adefovir,

amantadine, amprenavir, atazanavir, brivudine, capravirine, cidofovir, delavirdine, didanosine, efavirenz, emivirin, emtricitabine, enfurvirtide, famciclovir, fosamprenavir, foscarnet, ganciclovir, idoxuridine, indinavir, lamivudine, lopinavir, memantine, mozenavir, nelfinavir, nevirapine, oseltamivir, penciclovir, rimantidine, pentafuside, ritonavir, saquinavir, stavudine, tenofovir, tipranavir, trifluridine, valaciclovir, valganciclovir, zalcitabine, zanamivir, zidovudin, and the pharmaceutically acceptable salts thereof and mixtures thereof.

13. The method of claim 11, wherein the ribofuranose derivatives are 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the antiviral is acyclovir.

14. The method of claim 1 or 11 further comprising providing one or more further agents effective against an inflammatory bowel disease for simultaneous or successive administration with said derivative having Formula (I), wherein said further active agent is selected from the group consisting of anti-inflammatories, immunosuppressants, antibodies, antibody fragments, humanized monoclonal antibody against TNF-α, flavonoids, monoclonal antibodies against IL-12, monoclonal antibodies against IL-6, monoclonal antibodies against the α4β7 integrin receptor, keratinocyte growth factor, protein inhibitors of TNF-α, glucocorticoids, peptide analogues of glucagon-like peptide-2, glutathione peroxidase mimics, anti-sense TNF inhibitors, anti-sense ICAM-1 inhibitor, nitric oxide-releasing steroid derivatives, analogues of GLP-2, neurokinin-1 antagonists, NF-kappa-B inhibitors, orally-active phosphodiesterase IV inhibitors, thiazole derivatives, 5-lipoxygenase inhibitors, L-selectin antagonists, enzyme inhibitors, tryptase inhibitors, immunosuppressive macrolides, monoclonal antibodies against the α4β7 integrin receptor, glutathione peroxidase mimics, interferon, omega-3 fatty acids, inhibitors of cytokine synthesis, bactericidal/permeability agents, guanyl-hydrozone compounds, apoptotic antineoplastic drugs, thalidomide, recombinant interleukin-11 and mixtures thereof.

15. The method of claim 1, 11 or 14 further comprising providing inflixamab, wherein the ribofuranose derivative having Formula (I) and infliximab are administered to said subject as an admixture, separately and simultaneously, or separately in any order.

16. The method of claim 1, wherein said administration comprises parenteral administration, oral administration, inhalation, topical administration, transdermal administration, rectal administration, continuous infusion, or administration with an osmotic pump or a sustained release implant.

17. The method of claim 1, wherein said step of administering comprises orally administering the compound having Formula (I) in a dose between 100 mg and 1.5 g per day for one to four weeks.

18. The method of claim 17, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the inflammatory bowel disease is Crohn's disease

19. The method of claim 1, wherein the step of administering comprises:

(a) intravenously administering the compound having Formula (I) in a dose of about 10 to 40 mg/kg of body weight of the patient for about 20 to 45 minutes;

(b) intravenously administering the compound having Formula (I) in a dose of about 5 to 25 mg/kg of body weight of the patient every six hours for four days; and

(c) intravenously administering the compound having Formula (I) in a dose of about 2 to 15 mg/kg of body weight of the patient every six to eight hours for three days.

20. The method of claim 19, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the inflammatory bowel disease is Crohn's disease.

21. The method of claim 19, wherein the step of administering comprises:

(a) intravenously administering the compound having Formula (I) in a dose of 33 mg/kg of body weight of the patient for 30 minutes;

(b) intravenously administering the compound having Formula (I) in a dose of 16 mg/kg of body weight of the patient every six hours for four days; and

(c) intravenously administering the compound having Formula (I) in a dose of 8 mg/kg of body weight of the patient every eight hours for three days.

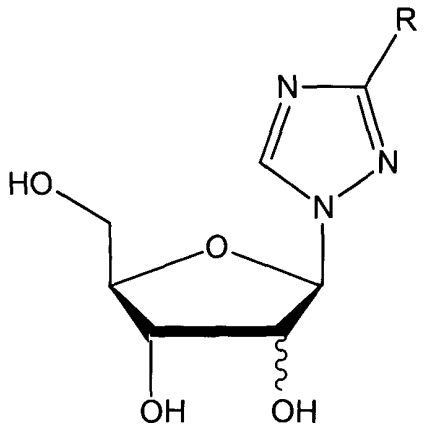
22. The method of claim 21, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the inflammatory bowel disease is Crohn's disease.

23. The method of claim 1, wherein the disease is selected from the group consisting of pseudomembranous colitis, hemorrhagic colitis, hemolytic-uremic syndrome colitis, collagenous colitis, ischemic colitis, radiation colitis, drug and chemically induced colitis, diversion colitis, ulcerative colitis, irritable bowel syndrome, irritable colon syndrome and Crohn's disease.

24. The method of claim 1, wherein the subject is a human.

25. The method of claim 10, wherein the agent is administered in an amount that is from about half the dosage to the same dosage which is, when administered alone, effective to treat or prevent said inflammatory bowel disease.

26. Use of one or more ribofuranose derivatives having the Formula (I):



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for the preparation of a medicament against an inflammatory bowel disease, wherein R is a group selected from the group consisting of a carboxamide, an amidine, and pharmaceutically acceptable acid addition salts thereof and the configuration at the C_2 carbon of the ribofuranose moiety is D or L.

27. The use according to claim 26, wherein the ribofuranose derivative having Formula (I) comprises one or more compounds selected from the group consisting of 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide, 1-β-L-ribofuranosyl-1H-1,2 4-triazole-3-carboxamide, 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine, 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine and pharmaceutically acceptable acid addition salts thereof.

28. The use according to claim 27, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide.

29. The use according to claim 27, wherein the ribofuranose derivative having Formula (I) is l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide.

30. The use according to claim 27, wherein the ribofuranose derivative having Formula (I) is l-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

31. The use according to claim 27, wherein the ribofuranose derivative having Formula (I) is l-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

32. The use according to claim 27, wherein the ribofuranose derivative is the hydrochloric acid addition salt of 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

33. The use according to claim 27, wherein the ribofuranose derivative is the hydrochloric acid addition salt of 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

34. The use according to claim 26, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and said inflammatory bowel disease is Crohn's disease.

35. The use according to claim 33, wherein said Crohn's disease is selected from the group consisting of active Crohn's disease, refractory Crohn's disease, and fistulizing Crohn's disease.

36. The use according to claim 26, wherein the ribofuranose derivative having Formula (I) is used in combination with at least one antiviral.

37. The use according to claim 36, wherein the antiviral is selected from the group consisting of abacavir, acyclovir, acyclovir sodium, acyclovir potassium, adefovir, amantadine, amprenavir, atazanavir, brivudine, capravirine, cidofovir, delavirdine, didanosine, efavirenz, emivirin, emtricitabine, enfurvirtide, famciclovir, fosamprenavir, foscarnet, ganciclovir, idoxuridine, indinavir, lamivudine, lopinavir, memantine, mozenavir, nelfinavir, nevirapine, oseltamivir, penciclovir, rimantidine, pentafuside, ritonavir, saquinavir, stavudine, tenofovir, tipranavir, trifluridine, valaciclovir, valganciclovir, zalcitabine, zanamivir, zidovudin, and the pharmaceutically acceptable salts thereof and mixtures thereof.

38. The use according to claim 36, wherein said ribofuranose derivatives are 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the antiviral is acyclovir.

39. The use according to claim 26 or 36, further comprising the use of one or more further active agents effective against inflammatory bowel disease, wherein said further active agent is selected the group consisting of anti-inflammatories, immunosuppressants, antibodies, antibody fragments, humanized monoclonal antibody against TNF-α, flavonoids, monoclonal antibodies against IL-12, monoclonal antibodies against IL-6, monoclonal antibodies against the α4β7 integrin receptor, keratinocyte growth factor, protein inhibitors of TNF-α, glucocorticoids, peptide analogues of glucagon-like peptide-2, glutathione peroxidase mimics, anti-sense TNF inhibitors, anti-sense ICAM-1 inhibitor, nitric oxide-releasing steroid derivatives, analogues of GLP-2, neurokinin-1 antagonists, NF-kappa-B inhibitors, orally-active phosphodiesterase IV inhibitors, thiazole derivatives, 5-lipoxygenase inhibitors, L-selectin antagonists, enzyme inhibitors, tryptase inhibitors, immunosuppressive macrolides, monoclonal antibodies against the α4β7 integrin receptor, glutathione peroxidase mimics, interferon, omega-3 fatty acids, inhibitors of cytokine synthesis, bactericidal/permeability agents , guanyl-hydrozone compounds, apoptotic antineoplastic drugs, thalidomide, recombinant interleukin-11 and mixtures thereof.

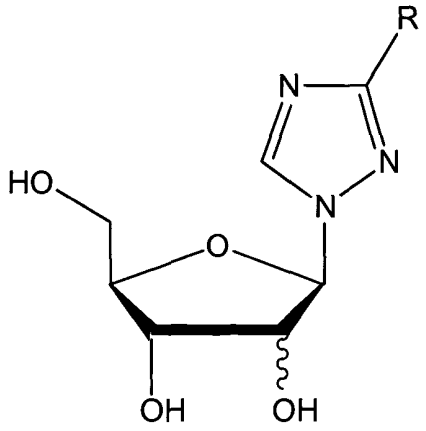
40. The use according to claim 26, 36 or 39, wherein the ribofuranose derivative having Formula (I) is used in combination with infliximab.

41. The use according to claim 26, wherein the medicament is formulated for parenteral administration, oral administration, inhalation, topical administration, transdermal administration, rectal administration, continuous infusion, or administration with an osmotic pump or a sustained release implant.

42. The use according to claim 26, wherein the disease is selected from the group consisting of pseudomembranous colitis, hemorrhagic colitis, hemolytic-uremic syndrome colitis, collagenous colitis, ischemic colitis, radiation colitis, drug and chemically induced colitis, diversion colitis, ulcerative colitis, irritable bowel syndrome, irritable colon syndrome and Crohn's disease.

43. A medicament for administration against an inflammatory bowel disease, comprising:

at least one ribofuranose derivative having the Formula (I):



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in an amount effective to treat or prevent said inflammatory bowel disease in a mammal, wherein R is a group selected from the group consisting of a carboxamide, an amidine and pharmaceutically acceptable acid addition salts thereof and the configuration at the C_2 carbon of the ribofuranose moiety is D or L.

44. The medicament of claim 43, comprising said ribofuranose derivative having Formula (I) in an amount between about 100 mg and 1.5 grams.

45. The medicament of claim 44, wherein said medicament is formulated for oral administration.

46. The medicament of claim 43, wherein said medicament is formulated for intravenous administration, parenteral administration, oral administration, inhalation, topical administration, transdermal administration, rectal administration, continuous infusion, or administration with an osmotic pump or a sustained release implant.

47. The medicament of claim 43, wherein the ribofuranose derivative having Formula (I) comprises at least one ribofuranose derivative selected from the group consisting of l-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide, 1-β-L-ribofuranosylH-1,2,4-triazole-3-carboxamide, 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine, 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine, and pharmaceutically acceptable acid addition salts thereof.

48. The medicament of claim 47, wherein the ribofuranose derivative having Formula (I) is l-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide.

49. The medicament of claim 43, wherein the ribofuranose derivative having Formula (I) is 1-β-L-ribofuranosylH-1,2,4-triazole-3-carboxamide.

50. The medicament of claim 43, wherein the ribofuranose derivative having Formula (I) is 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

51. The medicament of claim 43, wherein the ribofuranose derivative having Formula (I) is 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

52. The medicament of claim 43, wherein the ribofuranose derivative is the hydrochloric acid addition salt of 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

53. The medicament of claim 43, wherein the ribofuranose derivative is the hydrochloric acid addition salt of 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-amidine.

54. The medicament of claim 43, wherein the ribofuranose derivative having Formula (I) is l-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and said inflammatory bowel disease is Crohn's disease.

55. The medicament of claim 54, wherein said Crohn's disease is selected from the group consisting of active Crohn's disease, refractory Crohn's disease, and fistulizing Crohn's disease.

56. The medicament of claim 54, comprising said ribofuranose derivative having Formula (I) in an amount between about 100 mg and 1.5 grams.

57. The medicament of claim 56, wherein said medicament is formulated for oral administration.

58. The medicament of claim 43, further comprising one or more antivirals for administration simultaneously in admixture, separately and simultaneously, or separately in any order with said derivative having the Formula (I).

59. The medicament of claim 43 or 58, further comprising one or more further agents effective against an inflammatory bowel disease for administration simultaneously in admixture, separately and simultaneously, or separately in any order with said derivative having the Formula (I), wherein the further agent is selected the group consisting of anti-inflammatories, immunosuppressants, antibodies, antibody fragments, humanized monoclonal antibody against TNF-α, flavonoids, monoclonal antibodies against IL-12, monoclonal antibodies against IL-6, monoclonal antibodies against the α4β7 integrin receptor, keratinocyte growth factor, protein inhibitors of TNF-α, glucocorticoids, peptide analogues of glucagon-like peptide-2, glutathione peroxidase mimics, anti-sense TNF inhibitors, anti-sense ICAM-1 inhibitor, nitric oxide-releasing steroid derivatives, analogues of GLP-2, neurokinin-1 antagonists, NF-kappa-B inhibitors, orally-active phosphodiesterase IV inhibitors, thiazole derivatives, 5-lipoxygenase inhibitors, L-selectin

antagonists, enzyme inhibitors, tryptase inhibitors, immunosuppressive macrolides, monoclonal antibodies against the α4β7 integrin receptor, glutathione peroxidase mimics, interferon, omega-3 fatty acids, inhibitors of cytokine synthesis, bactericidal/permeability agents , guanyl-hydrozone compounds, apoptotic antineoplastic drugs, thalidomide, recombinant interleukin-11 and mixtures thereof.

60. The medicament of claim 59, wherein the further agent is in an amount that is from about half the dosage to the same dosage which, when the further agent is administered alone, is effective to treat or prevent said inflammatory bowel disease.

61. The medicament of claim 58, wherein said antiviral is selected from the group consisting of abacavir, acyclovir, acyclovir sodium, acyclovir potassium, adefovir, amantadine, amprenavir, atazanavir, brivudine, capravirine, cidofovir, delavirdine, didanosine, efavirenz, emivirin, emtricitabine, enfurvirtide, famciclovir, fosamprenavir, foscarnet, ganciclovir, idoxuridine, indinavir, lamivudine, lopinavir, memantine, mozenavir, nelfinavir, nevirapine, oseltamivir, penciclovir, rimantidine, pentafuside, ritonavir, saquinavir, stavudine, tenofovir, tipranavir, trifluridine, valaciclovir, valganciclovir, zalcitabine, zanamivir, zidovudin, and the pharmaceutically acceptable salts thereof and mixtures thereof.

62. The medicament of claim 58, wherein the ribofuranose derivatives are 1-β-D-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and 1-β-L-ribofuranosyl-1H-1,2,4-triazole-3-carboxamide and the antiviral is acyclovir.

63. The medicament of claim 43, wherein the disease is selected from the group consisting of pseudomembranous colitis, hemorrhagic colitis, hemolytic-uremic syndrome colitis, collagenous colitis, ischemic colitis, radiation colitis, drug and chemically induced colitis, diversion colitis, ulcerative colitis, irritable bowel syndrome, irritable colon syndrome and Crohn's disease.